

## **REMARKS**

### **I. Status of the Claims**

Claims 1-20, 22-39, 41, and 44-55 were pending at the time of mailing of the final Office Action. Claims 3-8, 11-20, 33-38 and 53-55 are presently withdrawn from consideration as being directed to a non-elected invention. Claim 1 been amended as set forth herein. Claims 23 and 29-30 have been canceled. New claim 57 has been added. New claim 57 is a member of the elected Group I invention, and support can be found in the specification generally, such as in figures 39-41 as originally filed. Support for the amendment to claim 1 can be found generally throughout the specification, such as in original claim 33 and on p.10 of the specification as filed. Claims 1-20, 22-28, 31-39, 41, and 44-57 are presently under consideration.

### **II. Claim rejections under §112**

The Action rejected claim 1 as indefinite due to the phrase “the formula further comprises R4”. In response, Applicants generally traverse; however, claim 1 has been amended in the interest of compact prosecution. Applicants submit that the rejection is moot in view of the instant amendments.

### **III. Claim rejections under §103**

Claims 1, 2, 9, 10, 24-28, 31-32, 41, and 44-52 are rejected under 35 U.S.C. §103(a) as being unpatentable over Arntzen *et al.* (U.S. Patent 6,444,233; hereinafter “Arntzen”) and further in view of Ni *et al.* (U.S. Patent 5,965,421; hereinafter “Ni”). In response, Applicants respectfully traverse.

Applicants note that claim 1 has been amended herein in the interest of compact prosecution to specify inflammatory bowel disease. Applicants submit that the previous declaration by Roger Anderson provides secondary considerations including *in vivo* data which is specifically relevant to inflammatory bowel disease. Although Applicants generally traverse

regarding the previous obviousness rejections directed towards embodiments involving rheumatoid arthritis, Applicants note that the instant claims have been amended in the interest of compact prosecution to specify inflammatory bowel disease. Applicants respectfully submit that the previous obviousness rejections directed towards rheumatoid arthritis are thus rendered moot.

As the Action acknowledges, Arntzen teaches compounds for treating inflammation. See Action p. 4. Applicants note that, as would be apparent to one of skill in the art, numerous causes of inflammation, including numerous inflammatory diseases, exist. Applicants note that the size of the prior art genus must be considered in an obviousness determination. See, e.g., Baird, 16 F.3d at 383, 29 USPQ2d at 1552. MPEP §2144.08. The very large number of inflammatory diseases and the lack of any express teaching of inflammatory bowel disease by Arntzen do not support a *prima facie* case of obviousness, particularly in view of the *in vivo* data previously provided in the declaration by Roger Anderson.

The Action alleges that the existence of inflammatory bowel disease as a cause of inflammation is sufficient to render the instant claims as obvious. The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. In re Baird, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994); In re Jones, 958 F.2d 347, 350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992). See also In re Deuel, 51 F.3d 1552, 1559, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995). MPEP§2144.08.

Applicants note that inflammatory bowel disease is currently typically treated with immunosuppression, surgery, or steroid treatment. The Action has not clearly articulated why one of skill, when considering the numerous possible causes of inflammation, would choose the particular disease, i.e., inflammatory bowel disease, to be combined with or treated by the particular compounds as instantly claimed. See MPEP § 2142 (explaining that the Action must provide a “clear articulation of the reason(s) why the claimed invention would have been

obvious"); *see also KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 401 (2007) (discussing the requirement to "determine whether there was an apparent reason to combine the known elements in the way a patent claims"); Examination Guidelines Update: Developments in the Obviousness Inquiry after *KSR v. Teleflex*, 75 Fed. Reg. 53648-49 (Sept. 1, 2010) (hereinafter "2010 Draft Obviousness Guidelines") (discussing the requirement to provide a clear articulation of the reasons the claims are rejected as obvious).

Applicants submit that the Action is using hindsight reconstruction based on Applicants disclosure to select a single pharmacological property of the instantly claimed compounds and a single disease, *i.e.*, IBD, from the numerous and often complex diseases and causes of inflammation. The use of hindsight to combine particular prior art elements in the manner claimed by Applicants is improper and cannot support an obviousness rejection. *See* MPEP § 2142 ("[I]mpermissible hindsight must be avoided."); *see also Grain Processing Corp. v. Am. Maize-Products Co.*, 840 F.2d 902, 907 (Fed. Cir. 1988) (In considering obviousness, "[c]are must be taken to avoid hindsight reconstruction by using 'the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit.'") (quoting *Orthopedic Equip. Co. v. United States*, 702 F.2d 1005, 1012 (Fed. Cir. 1983)).

The Action states on p. 4, "The composition would be expected to inhibit COX-2 since, iNOS and COX-2 are both mediators of inflammation..." Applicants contend this statement is speculative. The Action provides a citation (*i.e.*, US 5908861, col. 19, l. 62-65) in an attempt to support the above statement; however, this citation refers to an Example section which merely describes iNOS effects of a compound (*i.e.*, INH<sub>2</sub>BP) that is unrelated to the instantly claimed compounds, as well as the mechanism of action of pro-inflammatory cytokines. The Action has not provided any factual basis to assume that one of skill in the art would necessarily assume that

the instantly claimed compounds would exhibit a mechanism of action involving effects on COX-2. Applicants note that NF-kB is involved in a wide variety of cellular processes such as, e.g., stress, free radicals, oxidized LDL, viral infection, immune development, *etc.* The Action has not established that a person of ordinary skill would assume that the instantly claimed compounds would necessarily specifically affect COX-2 based only on an inhibition of NF-kB. The Action has not provided any prior citation describing actions of the instantly claimed compounds on COX-2. It is also unclear to Applicants whether the above statement is meant to indicate that the instantly claimed compounds would be expected to directly inhibit COX-2 (e.g., similar to ibuprofen) or indirectly affect COX-2 expression. It is believed that the above statement is unsupported conjecture with regard to the instantly claimed compounds. *See* MPEP § 2142 (“The examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. If the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness.” Emphasis added.). Nonetheless, Applicants submit that the above statement in the Action and the instant obviousness rejections are rendered moot in view of the instant amendments.

Applicants submit the obviousness rejections are rendered moot in view of the instant amendments and is not supported by a *prima facie* showing of obviousness as required by MPEP §2144.08, e.g., as in view of the previous declaration describing *in vivo* data obtained using an animal model of inflammatory bowel disease. The foregoing arguments also apply to the related Arntzen publication (WO 1999/59578) in view of Ni.

Applicants respectfully request that the rejection be withdrawn.

#### **IV. Nonstatutory Obvious-type Double Patenting**

Claims 1, 2, 9, 10, 21-32, 39-43, 46 and 48-51 are rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 and 16-21 of U.S.

Patent 6,962,720. The Examiner contends that while the conflicting claims are not identical, they are not patentably distinct from each other because the '720 patent and the rejected claims both recite methods of treating inflammation by administering a monoterpene.

In response, Applicants respectfully traverse. As noted above, the instant claims are drawn towards inhibiting inflammation in a subject with inflammatory bowel disease. Inflammatory bowel disease is not mentioned in the '720 patent. The Examiner has provided no factual evidence to support an obviousness rejection of the amended claims. *See* MPEP § 2142 ("The examiner bears the initial burden of factually supporting any *prima facie* case of obviousness."). Applicants note that there are many different types and causes of inflammation. Nothing in this reference teaches or suggests treating subjects with inflammatory bowel disease. Nor has the Examiner provided any evidence that treatment of inflammatory diseases are identical, and that all such diseases would be expected to respond in a similar manner to anti-inflammatory treatment. Thus, no *prima facie* case of obviousness has been established. Therefore, Applicants respectfully request that this rejection be withdrawn.

## **V. Conclusion**

In view of the foregoing, it is respectfully submitted that each of the pending claims is in condition for allowance, and a Notice of Allowance is earnestly solicited. The Examiner is invited to contact the undersigned agent at (512) 536-5674 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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